

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) A method for *in vivo* down-regulation of osteoprotegerin ligand (OPGL) activity in an animal, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of a modified OPGL polypeptide having general formula I:

$$(\text{MOD}_1)_{s1}(\text{OPGL}_{e1})_{n1}(\text{MOD}_2)_{s2}(\text{OPGL}_{e2})_{n2} \dots (\text{MOD}_x)_{sx}(\text{OPGL}_{ex})_{nx} \quad (\text{I})$$

-where OPGL_{e1} - OPGL_{ex} are x B-cell epitope containing subsequences of OPGL which independently are identical or non-identical and which optionally contain foreign side groups, x is an integer ≥ 3 , $n1$ - nx are x integers ≥ 0 of which at least one is ≥ 1 , MOD_1 - MOD_x are x modifications introduced between the preserved B-cell epitopes, and $s1$ - s_x are x integers ≥ 0 of which at least one is ≥ 1 if no optional side groups are introduced in the OPGL_e sequences, whereby the animal's own OPGL is down-regulated due to binding thereof to antibodies induced by immunization with the modified OPGL polypeptide, OPGL being a protein which acts as an osteoclast differentiation factor and which has an amino acid sequence as set forth in SEQ ID NO: 2 for human OPGL.

2. (Cancelled)

3. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide comprises at least one foreign T helper lymphocyte epitope (T_H epitope).

4. (Cancelled)

5. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide includes an amino acid substitution in or deletion in or insertion in or addition to the OPGL polypeptide sequence, or any combination thereof.

6. (Cancelled)

7. (Cancelled)
8. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide includes a duplication of at least one OPGL B-cell epitope.
9. (Previously Presented) The method according to claim 3, wherein the foreign T-cell epitope is immunodominant in the animal.
10. (Previously Presented) The method according to claim 9, wherein the foreign T-cell epitope is capable of binding to a large proportion of MHC Class II molecules.
11. (Currently Amended) The method according to claim 10, wherein the at least one foreign T-cell epitope is selected from the group consisting of a natural T-cell epitope and an artificial MHC-II binding peptide sequence.
12. (Currently Amended) The method according to claim 11, wherein the natural T-cell epitope is selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, and a *P. falciparum* CS epitope.
13. – 16. (Cancelled)
17. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide contains a modification in any one of positions 171-193, any one of positions 199-219, any one of positions 222-247, any one of positions 257-262, or in any one of positions 286-317, the amino acid numbering conforming with that of SEQ ID NO: 2.
18. (Original) The method according to claim 17, wherein the modification comprises a substitution of at least one amino acid sequence within a position defined in claim 17 with an amino acid sequence of equal or different length which contains a foreign T_H epitope.

19. (Previously Presented) The method according to claim 18, wherein the amino acid sequence containing the foreign T_H epitope substitutes amino acids 257-262 and/or 289-303 and/or 222-243 in SEQ ID NO: 2 or in a polypeptide where a cysteine corresponding to Cys-221 of SEQ ID NO: 2 has been substituted with Ser.

20. (Previously Presented) The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the modified OPGL polypeptide covalently or non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

21. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

22. (Currently Amended) The method according to claim 1, wherein an effective amount of the modified OPGL polypeptide is administered to the animal via a route selected from the group consisting of parenteral route selected from the group consisting of the intracutaneous, the subcutaneous, and the intramuscular routes; the peritoneal route; the oral route; the buccal route; the sublingual route; the epidural route; the spinal route; the anal route; and the intracranial route.

23. (Previously Presented) The method according to claim 22, wherein the effective amount is between 0.5 µg and 2,000 µg of the modified OPGL polypeptide.

24. (Previously Presented) The method according to claim 22, wherein the modified OPGL polypeptide is contained in a virtual lymph node (VLN) device.

25. – 27. (Cancelled)

28. (Currently Amended) The method according to claim 22, which includes at least one administration/introduction per year, such as at least 2, at least 3, at least 4, at least 6, and at least 12 administrations/introductions.

29. – 56. (Cancelled)

57. (Previously Presented) The method according to claim 1, wherein the animal is a human being.

58. (Previously Presented) The method according to claim 12, wherein the Tetanus toxoid epitope is a P2 or P30 epitope.

59. (New) The method according to claim 22, wherein the parental route is selected from the group consisting of the intracutaneous, the subcutaneous, and the intramuscular routes.

60. (New) The method according to claim 28, wherein the modified OPGL polypeptide is administered/introduced at least 2, at least 3, at least 4, at least 6 or at least 12 times per year.